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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,802	06/06/2001	Reiko M. Nakamura	10960-0112	2453

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,802	NAKAMURA, REIKO M.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears n the c ver sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *21-29* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's response filed 11/4/02 in Paper No. 5 is acknowledged and has been entered. Claims 1-20 have been cancelled. Claims 21-29 have been added. Accordingly, claims 21-29 are pending and are under examination.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings in this application are also objected to by the Draftsperson (see PTO-948 attached). Correction is required.

Specification

3. This application filed under former 37 CFR 1.60 lacks the necessary complete reference to the prior application. A statement reading, "This is a continuation of Application Serial No. 09/244,701, filed 2/4/1999, now abandoned, which claims the benefit of priority of Provisional Application No. 60/073,911 filed 2/6/1998 and Provisional Application No. 60/096,140, filed 8/11/1998" should be entered following the title of the invention or as the first sentence of the specification. The current status of all nonprovisional parent applications referenced should be included.

Trademark Usage

4. The use of the trademark "Toriiban", "Finn-chamber", "Perme-aide S" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 21-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is vague and indefinite in reciting, "the antigen composition is contained in the holding portion for transdermal delivery of the antigen" because it unclear how the antigen composition is contained or positioned in the holding portion so as to allow for transdermal delivery upon contact with skin.

Claim 21 lacks antecedent support in reciting, "the skin".

Claim 23 is vague and indefinite in reciting, " physiologically effective solution" because it is unclear how the solution is rendered "effective (physiologically)". Further, the term "effective" is a subjective term that lacks a comparative basis for defining its

metes and bounds. See also claim 27. It is further unclear how the physiologically effective solution promotes delivery of the antigen, i.e. transdermal or displacement.

In claim 28, "polyoxyethyene" should be "polyoxyethylene".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 21-23, 25-27, and 29 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Katsuhide et al. (JP 09206092, electronic translation version).

Katsuhide et al. disclose a transdermal delivery device comprising an antigen composition including a phosphate buffered solution for promoting transdermal delivery of the antigen, and a holding portion, i.e. plaster, which contains the antigen composition for use in delayed-hypersensitivity reaction measurement and wherein infectious disease such as tuberculosis by a tubercle bacillus, can be diagnosed therewith. The antigen is from isolated Mycobacterium bovis (BCG bacillus) culture. The mycobacterial antigens include MPB64, MPB59, MPB70, and MPB80. The antigen composition is formed into ointment, glycerol or polyethylene glycol then infiltrated into a strap or plaster for contact and application into skin of human or animal, i.e. patch test, to effect transdermal delivery of the antigen (see claims 5-8 and pages 4-5). After topical application of the ointment into skin by a patch, an allergic reaction in the form of

a hardening phenomenon on the skin area is caused by the existence of antibody to said mycobacterial antigens (see page 3, lines 3-10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Katsuhide et al. (JP 09206092, electronic translation version) in view of (1) Haga et al. (Tubercle and Lung Disease, June 1994, Supp. No. 1(196)) or (2) Haga et al. (Jpn. J. Med. Sci. Biol, 1996).

Katsuhide et al. disclose a transdermal delivery device comprising an antigen composition including a phosphate buffered solution for promoting transdermal delivery of the antigen, and a holding portion, i.e. plaster, which contains the antigen composition for use in delayed-hypersensitivity reaction measurement and wherein infectious disease such as tuberculosis by a tubercle bacillus, can be diagnosed therewith. The antigen is from isolated Mycobacterium bovis (BCG bacillus) culture. The mycobacterial antigens include MPB64, MPB59, MPB70, and MPB80. The antigen composition is formed into ointment, glycerol or polyethylene glycol then infiltrated into a strap or plaster for contact and application into skin of human or animal, i.e. patch test,

to effect transdermal delivery of the antigen (see claims 5-8 and pages 4-5). After topical application of the ointment into skin by a patch, an allergic reaction in the form of a hardening phenomenon on the skin area is caused by the existence of antibody to said mycobacterial antigens (see page 3, lines 3-10).

Katsuhide et al. fail to that the antigen is derived from mycobacteria such as *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellulare, Mycobacterium kansaii, Mycobacterium fortuitum, Mycobacterium chelonae, Mycobacterium leprae, Mycobacterium africanum, and Mycobacterium microti*, as recited in claim 3.

(1) Haga et al. teach a mycobacterial protein, MPB64 which is isolated from Mycobacterium bovis. (1) Haga et al. further teach that MPB64 gene is also detected in other mycobacterial species via polymerase chain reaction such as *Mycobacterium tuberculosis*, *Mycobacterium africanum, and Mycobacterium microti*. Another mycobacterial antigen, MPB70 protein, likewise, has the same distribution pattern as MPB64.

(2) Haga et al. disclose mycobacterial antigen MPB64, a secretory protein isolated from M. bovis culture filtrate which corresponds to the secretory protein isolated from M. tuberculosis denoted as MPT64. Both MPB64 and MPT64 have identical protein structure on the basis of gene analysis and are therefore designated as MPB/T64, hereinafter, referred to as MPB64. MPB64 is highly specific to M. tuberculosis complex and is, therefore, an ideal antigen for diagnosis of tuberculosis (see Introduction). In their studies, (2) Haga et al. showed that detection of MPB64 by

delayed skin reaction correlated well with development of tuberculosis in guinea pigs (see page 25 and Figures 6 and 7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to isolate, derive, and identify MPB64 from other mycobacterial species such as *M. tuberculosis, M. africanum and M. microti* such as taught by (1) Haga for incorporation into the transdermal delivery device taught by Katsuhide, because (1) Haga specifically isolated MPB64 from *M. tuberculosis, M. africanum, and M. microti* using PCR. Further, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of (2) Haga into the teaching of Katsuhide because (2) Haga specifically taught that MPT64 of M. tuberculosis and MPB64 of M. bovis (also taught by Katsuhide) have identical protein structures and have a high specificity to M. tuberculosis complex. Given the teaching that delayed skin reaction observed in guinea pigs correlates well with the development of tuberculosis, one of ordinary skill in the art would have been motivated to incorporate the teaching of (1) Haga or (2) Haga into the transdermal delivery device of Katsuhide because it allows for accurate diagnosis of tuberculosis infection in humans without the need for invasive procedures.

8. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Katsuhide et al. (JP 09206092, electronic translation version) in view of Barchfield et al. (US 5,709,879).

Katsuhide has been discussed supra. Katsuhide et al. differ from the instant invention in failing to teach polyoxyethylene sorbitan derivative as surfactant for use in the instant invention.

Barchfield et al. disclose a combination of adjuvant components, i.e. liposome/antigen component and emulsion component which act together to produce elevated immune response which is useful in delivering antigens to cells and inducing immunity against said antigen (pathogen) or measuring specific reactivity of antibodies against said antigen. Barchfield et al. disclose that a composition of antistimulatory agent comprising antigen, i.e. killed M. tuberculosis, mixed with mineral oil and emulsifying agent is currently known as complete Freund's adjuvant but is known to cause severe side effects. Barchfield et al. then teach using preferred surfactants designed for and commonly used in biological situations; these include polyoxyethylene sorbitan fatty acid ethers sold under the trade name TWEEN, and sorbitan fatty acid ethers sold under the trade name SPAN. These surfactants are sorbitan-based and non-ionic prepared by dehydration of sorbitol, reaction with fatty acid, then reaction with ethylene oxide, i.e. sorbitan monolaureate, sorbitan monopalmitate, sorbitan monostearate, sorbitan monooleate, sorbitan sesguioleate, and sorbitan trioleate which are commercially available under the trademark name TWEEN. TWEEN 80 or polysorbate 80 or polyoxyethylene sorbitan monooleate, is most useful in preparing oil-in-water emulsions and dispersions and solubilizing oils and making anhydrous ointments water-soluble or washable. Antigen masses are selected based on desired dose and volume of the final composition and are adjusted depending on the

immunogenic response. The ability of antibodies to distinguish a specific antigenic structure has resulted in their wide use in diagnosis (see columns 15 and 16 and Example 8).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the surfactant in the teaching of Barchfield into the physiologically effective solution in the transdermal delivery device as taught by Katsuhide because Barchfield specifically taught that polyoxyethylene sorbitan surfactants are commercially known and conventional in emulsifying agents applicable in adjuvant combinations such as those infiltrated into the transdermal delivery device taught by Katsuhide.

9. No claims are allowed.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Haga et al.(Journal of Leucocyte Biology, (February 1995)) teach that because MPB64 is secreted only by living M. tuberculosis and some strains of BCG, it can be used for diagnosing tuberculosis.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703)

305-0807. The examiner can normally be reached on Monday to Friday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays at 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
Patent Examiner
Art Unit 1641 GG 1/6/03

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641